



A NOVEL SYNTHESIS AND ANTIMICROBIAL STUDIES OF N-(7-SUBSTITUTEDTHIOCARBAMIDOQUINOLINE-4-YL)- N,N-DIETHYL-PENTANE-1,4-DIAMINE

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ABSTRACT

Thioamido, quinilino, benzamido and benzoido group containing heterocycles created their own identity and importance in pharmaceutical, medicinal, agricultural and drug sciences. Thioamido and benzamido heterocyclic compounds showed noticeable and remarkable applications in industrial, pharmaceutical, medicinal and drug chemistry. Hence taking all these facts into consideration it was thought interesting to synthesize N-(7-substitutedthiocarbamidoquinoline-4-yl)-N,N-diethyl-pentane-1,4-diamines by interacting N-(7-chloroquinoline-4-yl)-N,N-diethyl-pentane-1,4-diamine with various thiourea in isopropanol medium. The justification and identification of the structure of these newly synthesized compounds had been established on the basis of chemical characterization, elemental analysis and through spectral data. The antimicrobial activities of these compounds were screened against *E. coli*, *S. typhi*, *S. abony*, *P. aeruginosa*, *B. subtilis*, *A. niger*, and *C. albicans* pathogens which are hitherto unknown.

Keywords: Substitutedthiocarbamides, N-(7-substitutedthiocarbamidoquinoline-4-yl)-N, N-diethyl-pentane-1,4-diamine and isopropanol

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INTRODUCTION

Recently in this laboratory the synthetic applications of cynoguanidine and 1,3-diformamido-thiocarbamide had been briefly explored¹. As evident from structure of N-(7-substitutedthiocarbamidoquinoline-4-yl)-N,N-diethyl-pentane-1,4-diamine processes chloro, amino, methyl and ethyl reactive sides for various reactions. As a wider programme of this laboratory in the synthesis of nitrogen, sulphur and nitrogen and sulphur containing heterocycles and heterocycles the interactions of cynoguanidine with various thioureas and isothiocyanates had been investigated in sufficient details²⁻⁸. Some of these compounds showed remarkable pharmaceutical and biological activities⁹⁻¹².

An exhaustive literature survey showed that thiocarbamido³⁻⁶ and N-(7-substitutedthiocarbamidoquinoline-4-yl)-N,N-diethyl-pentane-1,4-diamine¹³⁻¹⁵ containing drugs play an important role in pharmaceutical, medicinal and drug chemistry having remarkable pharmaceutical, medicinal and biochemical applications. By considering all these facts, interactions of N-(7-chloroquinoline-4-yl)-N,N-diethyl-pentane-1,4-diamine with various thiourea in isopropanol medium were investigated to isolate yet new series of N-(7-substitutedthiocarbamidoquinoline-4-yl)-N,N-diethyl-pentane-1,4-diamines (Scheme 1) and antimicrobial activities were studied.

EXPERIMENTAL

The melting points of the all synthesized compounds were recorded using hot Paraffin bath. The carbon and hydrogen analysis were carried out on Carlo-Ebra 1106 analyzer. Nitrogen estimation was carried out on Colman-N-analyzer-29. IR spectra were recorded on Perkin Elmer Spectrometer in range 4000-400 cm⁻¹ in KBr pellets. PMR spectra were recorded on Bruker Ac 300 F Spectrometer with TMS as internal

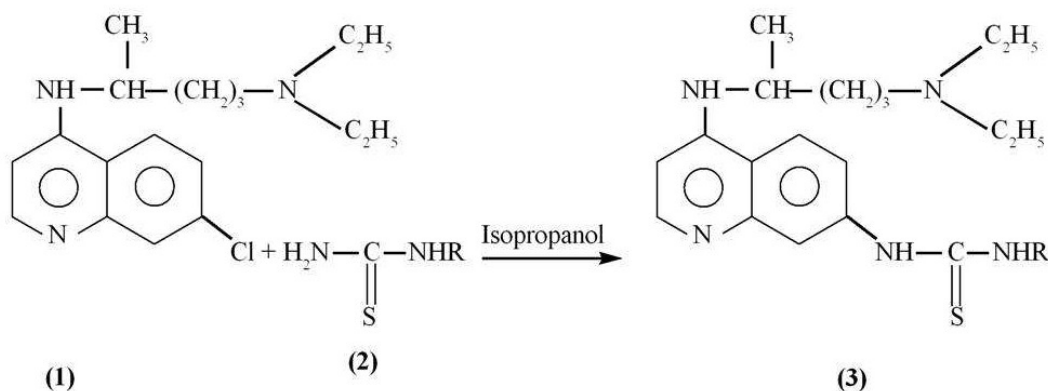
standard using CDCl_3 and $\text{DMSO}-d_6$ as solvent. The purity of compound was checked on silica Gel-G Pellets by TLC with layer thickness of 0.3 mm. All chemicals used were of AR-grade.

N-(7-thiocarbamidoquinoline-4-yl)-N, N-diethyl-pentane-1, 4-diamine

A mixture of N-(7-chloroquinoline-4-yl)-N, N-diethyl-pentane-1, 4-diamine (1a) (0.1M), thiourea (2a) and isopropanol (40ml) was refluxed on boiling water bath for 4 hrs. During boiling suspended N-(7-chloroquinoline-4-yl)-N, N-diethyl-pentane-1, 4-diamine went into the solution and the new product was found to be gradually separated out. Which on basification with dilute ammonium hydroxide afforded crystals. It was filtered in hot condition and crystallized with aqueous ethanol to obtain (3a), yield 67.7%, melting point 196°C . (D)

Properties

It is white, crystalline solid having melting point 196°C . (D). It gave positive test for nitrogen and sulphur. Desulphurised with alkaline plumbite solution. It formed picrate, melting point 120°C .



Where R = -H, -phenyl, -methyl, -ethyl, -allyl

Scheme-1

Elemental analysis

C [(found 66.4%) calculated 68.92], H [(found 7.28%) calculated 7.58%], N [(found 15.21%) calculated 16.15], S [(found 6.72%) calculated 7.35].

IR Spectra The IR spectra was carried out in KBr pellets and The important absorption can be correlated as (cm^{-1}) 3435.6 (N-H stretching), 3150.5 [C-H(Ar) stretching], 1638.1 (C-N stretching), 1523.6 ($=\text{C}=\text{NH}$ imino), 1199.7 (C-N stretching), 991.9 ($\text{N}=\text{C}=\text{S}$).

PMR Spectra The spectrum was carried out in CDCl_3 and $\text{DMSO}-d_6$. This spectrum distinctly displayed the signals due to Ar-H, protons at $\delta 7.9525\text{--}7.9543$ ppm. Ar-NH protons at $\delta 5.0417\text{--}5.0483$ ppm, pyrimidino-NH at $\delta 4.2911\text{--}4.4564$ ppm. $-\text{CH}_2$ protons at $3.3386\text{--}3.8638$ ppm. $-\text{CH}_3$ protons at 1.2538 ppm. Similarly other N-(7-substitutedthiocarbamidoquinoline-4-yl)-N,N-diethyl-pentane-1,4-diamines were synthesized by above mentioned method and are mentioned in Table-1.

Table-1

S.No.	Expt. No.	N-(7-Substituted Thiocarbamidoquinoline-4-yl)-N, N-diethyl-pentane-1,4-diamine	Yield %	m.p. $^\circ\text{C}$
3b	2	 -Phenyl.....	67	171
3c	3	Methyl.....	75	167
3d	4	-Ethyl.....	78	180
3e	5	Allyl.....	65	178

Antimicrobial and Antifungal Activities

The antimicrobial and antifungal activities¹⁶ of all these compounds were screened by using cup-plate agar diffusion method in DMF, using standard Co-Trimazin 25 µg/ml against gram positive and gram negative bacteria such as *E. coli*, *S. typhi*, *S. abony*, *P. aeruginosa*, and *B. subtilis*. While all compounds were also screened for their antifungal activities by using standard Greseofulvin (10µg/ml) against *A. niger* and *C. albicans*.

Cup-plate method

A medium used throughout the experiment was HI-Media (India make) having composition of Pepton-5gm/lit., NaCl -5gm/lit, Yeast extract -1.5gm/lit, Agar powder -20gm/lit, p^H - 7.4 ± 0.1

The medium for antibacterial and antifungal activities were prepared [N-agar for bacterial and Sabourands dextrose agar for fungi] by dissolving 26 gms of ingredients in one liter of distilled water and sterilized in autoclave at 121 °C at 15 lbs/inch pressure in an autoclave for 154 minutes. Then microbes were inoculated with requisite quantity to the medium at temperature 40-50°C and immediately poured the inoculate medium in to sterilized petridishes to give a depth of 3-4 mm of uniform thickness. After solidification the well or holes were prepared by well borer. The dimethylformamide solution of the compound was added in sufficient amount to fill the well. Then it was kept at room temperature for 4 h, as a pre-incubation and then plates of bacteria were inoculated for 18-24 hrs, at 36-38°C and all plates fungi were inoculated 48 hrs at 20-25 °C. After the period of inoculation, zones of inhibition were recorded around the wells. The results are cited in Table-2.

Table-2

Comp. No.	<i>S.typhi</i> (mm)	<i>E.coli</i> (mm)	<i>S. abony</i> (mm)	<i>P.aeruginosa</i> (mm)	<i>B. subtilis</i> (mm)	<i>A. niger</i> (mm)	<i>C. albicans</i> (mm)
3a	1.2	1.0	1.2	0.8	0.4	--	--
3b	1.8	1.6	1.8	1.1	1.2	0.3	--
3c	1.4	1.1	1.1	0.7	0.6	--	--
3d	1.1	0.9	0.6	0.6	0.6	0.1	--
3e	1.6	1.2	1.3	1.0	0.8	--	--

All the seven organisms studied are human pathogens from the results it is clear that all the synthesized compounds showed remarkable and considerable antimicrobial activities. These thiocarbamides showed highly activity against *E. coli*, *S. typhi*, *S. abony*, *P. aeruginosa*, *B. subtilis*, While less active against *A. niger* and *C. albicans*. Hence study of this compounds is required in biochemical and medicinal directions. From the above data it is concluded that this compounds showed remarkable antibacterial activity that antifungal activity. *S. typhi* causes typhoid while *E. coli* causes diarrhoea and *S. abony* causes pus formation. It is observed from literature survey of medicinal sciences that in the last two decades the patients of typhoid and diarrhoea throughout the world are common. Lower drugs of typhoid are now totally rejected and higher drugs are now given to the patients. As newly synthesized thiocarbamides showed remarkable and considerable activities so these compounds can be used as alternative for the treatment of diseases caused by the above mentioned pathogens only if they do not have toxic and other side effects after the details study. The potency of the drug is increased due to substitution of thiocarbamido moiety on the previous drug.

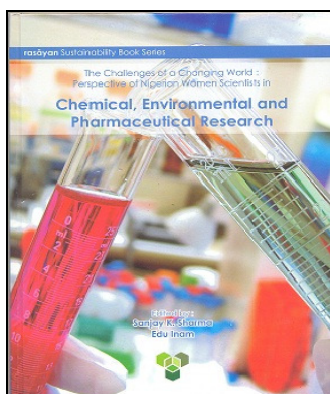
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